MEDICAL PROCEEDINGS

MEDIESE BYDRAES

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EDITORIAL · REDAKSIONEEL

ADMISSION TO OUR MEDICAL SCHOOLS

The National Bureau of Educational and Social Research recently published *A Survey of the Training and Employment of Scientists and Engineers in South Africa.* Chapter 4 (Part 5) dealt with *The Training and Employment of Medical, Dental and Auxiliary Medical Personnel.* The full text of this chapter was published in *Medical Proceedings* on 13 August 1960 at p. 347.

The considered conclusion reached by the authors of the Survey was that there would be a shortfall of some 2,000 doctors by 1965 and that there appeared 'to be need for considerable concern in this connexion.' The conclusions about the shortage of medical manpower in South Africa have remained virtually unchallenged. They emphasize the urgency of increasing the intake of medical students to cope with the country's requirements. The problem may partly be solved by extending the existing facilities for teaching; but this stratagem is unlikely to meet the requirements of the situation. More medical schools are clearly needed.

We may have to adopt a more flexible attitude in adapting and extending existing facilities for undergraduate training. There is no reason why, in an area such as Johannesburg, the peripheral hospitals could not be staffed with teaching units under the administrative direction of the University of the Witwatersrand. There is a plenitude of profes-

TOELATING TOT ONS MEDIESE SKOLE

Die Nasionale Buro vir Opvoedkundige en Maatskaplike Navorsing het onlangs *'n Opname van die Opleiding en Indiensneming van Wetenskaplikes en Ingenieurs in Suid-Afrika* gepubliseer. Hoofstuk 4 (Deel 5) handel oor *Die Opleiding en Indiensneming van Mediese, Tandheelkundige en Mediese Hulppersoneel.* Hierdie hele hoofstuk is onverkort op 13 Augustus 1960 in *Mediese Bydraes* gepubliseer (bl. 347).

Die oorwoë gevolgtrekking waartoe die opstellers van die Opname geraak het, was dat daar teen 1965 'n tekort van ongeveer 2,000 dokters sal wees, en dat daar oënskynlik rede vir heelwat besorgdheid in hierdie verband bestaan. Die gevolgtrekking oor die tekort aan mediese werkkragte word deur feitlik niemand betwis nie, en beklemtoon die noodsaaklikheid vir die toelating van meer mediese studente om in die land se behoeftes te voorsien. Dit is moontlik dat die probleem gedeeltelik opgelos kan word deur 'n uitbreiding van die bestaande onderrigfasiliteite, maar dit is onwaarskynlik dat so 'n plan aan al die behoeftes van die toestand sal kan voldoen. Dit is duidelik dat meer mediese skole nodig is.

Bes moontlik sal ons 'n meer buigbare houding moet aanneem wat betref die aanpassing en uitbreiding van die bestaande fasiliteite vir die opleiding van ongegradueerdes. Daar is geen rede waarom, in 'n gebied soos Johannesburg, die buitehospitale nie voorsien

sional talent in all our major centres who would be glad to assist in such a teaching programme on a full-time or a part-time basis, or in an honorary capacity.

In addition, the advantage of modern methods of communication should be exploited. It has been the distressing experience of every medical practitioner that only the geographically favoured few in the front row, whether in the autopsy room or at the bedside, see much of what is being demonstrated. As we have recently had proved to us by the Smith Kline and French Organization, colour television as a teaching technique would bring every demonstration to the immediate and complete notice of every student. The use of colour television as a teaching aid would remove an enormous burden of routine drudgery from the teaching staff and would make the demonstration available to almost unlimited numbers of spectators. Television does not, however, eliminate the need for the student personally to examine the patient. It is for this reason that the peripheral hospitals should be embraced in the academic fold.

Existing limitations on the admission of students have led to some form of screening. It must be recognized at once that there is no test whereby the future medical practitioner can be picked out with any prospect of success. It does not follow that academic attainment of a high order in the matriculation examination is a passport to competent medical practice. In any event, it may be preferable to retain a variety of abilities and characters among the young men and women prepared to devote themselves to medicine as a career. We need doctors for teaching and research as well as institutional and private practice. This implies a variegated set of talents and personalities. The best test for admission is the desire of the matriculant to submit himself to the rigours of a 7-year course of training. Any attempt to select on any other basis must not merely reflect the prejudices of the selectors.

Admission to medical training should be a right and not a privilege, in the same way as general education in the 3 R's is to-day regarded as a right and not a privilege. From the numbers coming forward it is evident that there is a great body of dedicated young South Africans prepared to make medicine their vocation. We must find room to absorb such persons into our medical schools.

Our medical schools should be also mindful of the Hippocratic Oath to which, as a profession, we subscribe:

'. . . I will keep this Oath and this stipulation —to reckon him who taught me this Art equally

kan word van onderrigeenhede wat onder die administratiewe leiding van die Universiteit van die Witwatersrand optree nie. Daar is 'n oorvloed van begaafde professionele manne in al ons vernaamste stede wat maar te bly sal wees om op 'n voltydse of deeltydse grondslag, of in 'n ere-hoedanigheid, met so 'n onderrigprogram te help.

Daarbenewens behoort die voordele van moderne metodes van kommunikasie ondersoek te word. Elke mediese praktisyn weet uit onrusbarende ondervinding dat slegs die aardrykskundig begunstigde enkeles in die voorste ry, of dit nou al in die outopsiesaal of in die siekekamer is, veel kan sien van wat gedemonstreer word. Soos daar onlangs aan ons bewys is deur die organisasie Smith, Kline & French, kan kleurbeeldradio as onderrigtegniek elke demonstrasie onder die onmiddellike en algehele aandag van die elke student bring. Die gebruik van kleurbeeldradio as 'n onderrighulpmiddel sal die enorme las van roetinesleurwerk van die skouers van die onderrigpersoneel verwyder, en sal die demonstrasie tot beskikking van 'n haas onbeperkte aantal toeskouers stel. Die noodsaaklikheid vir die student om die pasiënt persoonlik te ondersoek, word egter nie deur beeldradio uitgeskakel nie. Dit is om hierdie rede dat die buite hospitale in die akademiese kraal opgeneem behoort te word.

Die bestaande beperkinge op die toelating van studente het reeds aanleiding tot 'n sekere mate van keuring gegee. Daar behoort egter dadelik erken te word dat daar geen toets is waarvolgens die toekomstige mediese praktisyn met enige hoop op welslae gekies kan word nie. Dit is beslis nie waar dat akademiese prestasies van 'n hoë orde in die matrikulasie-eksamen 'n paspoort tot 'n geslaagde mediese praktyk is nie. In elk geval is dit miskien verkieslik om 'n verskeidenheid van bekwaamhede en karaktertrekke te bewaar onder die jong manne en vroue wat bereid is om hulself aan die geneeskunde as 'n loopbaan te wy. Ons het dokters vir onderrig en navorsing net so nodig as wat ons dokters vir intigtings en vir die private praktyk het. Dit vereis 'n hele verskeidenheid van begaafdhede en persoonlikhede. Die beste toets vir toelating is die verlange aan die kant van die matrikulant om homself aan die veeleisende 7-jarige opleidingskursus te onderwerp. Enige poging om 'n keuse op enige ander grondslag te doen, moet nie bloot 'n weerspieëling van die vooroordeel van die keurders wees nie.

Toelating tot mediese opleiding behoort 'n reg te wees, nie 'n voorreg nie, net soos algemene opleiding in die lees-, skryf- en rekenkuns vandag 'n reg en nie 'n voorreg is nie. Geoordeel aan die aantal wat hulle aanmeld, is dit duidelik dat daar 'n groot en toegewyde groep jong Suid-Afrikaners is wat die geneeskunde hul loopbaan wil maak. Ons moet plek vind om hierdie persone in ons mediese skole op te neem.

Ons mediese skole behoort ook gedagtig te bly

dear to me as my parents, to share my substance with him, and relieve his necessities if required; to look upon his offspring on the same footing as my own brothers, and to teach them this Art, if they shall wish to learn it, without fee or stipulation; and that by precept, lecture, and every other mode of instruction, I will impart a knowledge of the Art to my own sons, and those of my teachers, and to disciples bound by a stipulation and Oath according to the law of medicine, but to none others . . .'

The Hippocratic Oath underlines something which tends to be forgotten, viz. that there is a special obligation on the part of our medical schools to make provision for the children of medical practitioners who wish, in their turn, to follow in their fathers' footsteps. It seems improper not to set aside a percentage of new admissions for the sons of doctors. Such candidates with a medical background in their families know what the career entails and they should not be barred by a criterion which is no test of their suitability or future success. Selectors need to be particularly mindful of the special consideration which should be shown to such candidates; and they should guard against the temptation of building medical schools in their own image.

aan die Hippokratiese Belofte wat deur ons as 'n professie afgelê is:

'. . . Ek sal hierdie eed getrou nakom, asook hierdie bepaling—om hom wat my hierdie kuns geleer het net soveel soos my ouers te bemin, om wat ek besit met hom te deel, en, indien nodig, in sy behoeftes te voorsien; om sy kinders soos my eie broers te beskou en om hulle in hierdie kuns te onderrig as hulle dit wil leer, sonder geldelike beloning of voorwaardes; en dat ek deur voorbeeld, lesings en alle ander onderrigmetodes 'n kennis van die kuns sal oordra aan my eie seuns, en aan dié van my leermeesters, sowel as aan dissipels gebonde deur 'n bepaling en eed, ooreenkomstig die wet van die geneeskunde, maar aan geen ander nie . . .'

Die Hippokratiese Belofte beklemtoon iets wat ons geneig is om te vergeet, naamlik dat daar 'n spesiale verpligting op ons mediese skole rus om voorsiening te maak vir die kinders van mediese praktisyns wat, op hul beurt, in hul vaders se voetspore wil volg. Dit skyn verkeerd te wees om nie 'n sekere persentasie van die nuwe toelatings tot ons mediese skole vir die seuns van dokters voor te behou nie. Hierdie kandidate met 'n mediese familieagtergrond weet maar al te goed wat so 'n loopbaan vereis, en hulle behoort nie uitgesluit te word deur 'n toets wat geen maatstaf van hul geskiktheid of toekomstige welslae is nie. Keurders moet veral gedagtig bly aan die spesiale oorweging wat hierdie kandidate verdien, en hulle behoort te waak teen die versoeking om mediese skole volgens hule eie beeld op te bou.

ABSTRACT

ACUTE AMOEBIC DYSENTERY

TREATMENT WITH ENTAMIDE FUROATE

The authors report from Tanganyika on a clinical trial carried out with Entamide Furoate (Furamide). The drug was used in 5-day courses for the treatment of acute amoebic dysentery and 50 patients (44 inpatients and 6 outpatients) were treated over a period of 8 months. The dosage consisted of 500 mg. 3 times daily for 5 days for adults and 25 mg. per Kg. body weight daily for 5 days for children. (The manufacturers recommend that Entamide Furoate should be administered for a 10-day course). All the patients were Africans or Arabs from the Morogoro district of Tanganyika where there is a high incidence of acute amoebic dysentery and hepatitis. Patients with amoebic hepatitis were not included in the trial and all patients were passing *E. histolytica* trophozoites in the stools and all except 2 had diarrhoea. These 2 patients complained of blood-stained stools and abdominal pain.

On the 6th and 7th days after the commencement of treatment saline preparations of fresh stools were examined. Patients were classified as cured if they had no diarrhoea and if the stools were not found to contain either *E. histolytica* cysts or trophozoites. All patients were instructed to return for follow-up examinations at monthly intervals.

Of the total of 50 patients treated (32 men, 13 women and 5 children), 45 were considered cured on the 7th day and 5 were regarded as failures. Three patients developed recurrences of acute amoebic dysentery within 3 months of treatment and 2 patients had a recurrence or re-infection occurring later than 3 months after treatment. Of the 5 patients regarded as failures after 5 days' treatment with Entamide Furoate, one was absolutely cured after a fresh course of 5 days with the drug, and a child of 1 year who failed to respond after 5 days did so with a further course of 5 days at a higher dosage of 60 mg. per kg. body weight. Of the 5 patients with recurrences or re-infections, 4 were successfully treated with a further 5-day course of Entamide Furoate but the 5th was given emetine and emetine bismuth iodide as Entamide Furoate was not available.

As is usual in a trial of this type, the follow-up of cases was disappointing. The excessive flatulence previously reported with this drug did not occur in this trial. One patient complained of mild dysphagia during treatment and another complained of a sore tongue which appeared normal on examination. One female patient had menorrhagia which the authors considered to be due to the diarrhoea and pelvic congestion.

The authors concluded that Entamide Furoate gave a presumptive cure rate of 90% in acute amoebic dysentery and was cheap, non-toxic and safe for use in outpatients.

[Haddock, D. R. W. and Mgaya, J. K. N. (1961): East Afr. Med. J., **38**, 374.]

THE ROLE OF CHOLESTEROL IN CORONARY ARTERY DISEASE

ALTERATIONS IN THE SERUM LIPIDS

FOLLOWING THE USE OF TRIPARANOL (MER 29)

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Although, in the past, coronary thrombosis was regarded as the sole cause of the condition now termed myocardial infarction, it is now recognized that thrombosis is not the only cause of coronary occlusion. Many workers investigating cases of myocardial infarction have noted that thrombosis is present in only one third to one half of such cases.[1-3]

Leary[4] suggests that the primary lesion of coronary atherosclerosis arises in the intima and that 4 stages of lipoidosis, phagocytosis, fibrosis and necrosis may be distinguished.

In the first stage, there is a deposition of lipid underneath the epithelium of the intima and phagocytosis occurs, the phagocytes forming the so-called 'foam cells' which arise in the subendothelial layer and stimulate the production of fibrosis, focal or diffuse. The resultant plaque is frequently crescentic since the lesion does not often encircle the artery. Finally, an accumulation of the lipid cells combined with inadequate supporting tissue and poor vascularization results in necrosis and consequent lymphoid infiltration.

Other workers[5-7] suggest that the primary lesion is in the media but all agree that the initial pathological change consists of the deposition of lipid.

It is therefore apparent that an excess deposition of lipids must be regarded as the starting point of generalized atheroma and coronary artery disease. The rather loose term 'lipids' covers a number of fatty substances which are dissimilar in nature but are all extractable by fat solvents and include the neutral fats, fatty acids, phospholipids and cholesterol. Attention was particularly concentrated upon the role of cholesterol following the work of Anitschkow[8] in 1925 on the production of atheroma in rabbits by the feeding of cholesterol. Since that time the results of many animal experiments have confirmed his findings, but it must be pointed out, in passing, that these investigations were carried out on herbivorous animals whose feeding habits and metabolism bear little relation to those of man.

Cholesterol has probably assumed an undue degree of importance in coronary artery disease because its estimation is relatively simple in comparison with the other 'lipids.' The work of Bottcher *et al.*[9] on the analysis of human aortas has demonstrated that unsaturated fatty acids are increased to a level comparable with that of cholesterol and must be considered similarly implicated as etiological factors.

Oncley *et al.*[10] have pointed out that the beta lipoproteins are not concerned with the transport of fats to and from the fat depots, but are carriers to the cells of specialized molecules elaborated by the liver. By linkage with the polypeptides, the lipids are rendered water soluble and are freely transported in the blood stream preparatory to the deposition of lipids in cells for their metabolism. Therefore only the protein-carried cholesterol need be considered as an etiological factor, as its linkage to the beta proteins can be ruptured easily. In the body, cholesterol is present mainly in the form of cholesterol esters and hence acts as a vehicle for fatty acids which Bloor *et al.*[11] have demonstrated to be selected from the most unsaturated fatty acids.

Kayahan[12] has postulated, in coronary artery disease, an increased affinity of the beta proteins for lipids and it would appear that this 'supersaturation' leads to a ready deposition of such lipids in the arterial walls. It will therefore be appreciated that there are two schools of thought with regard to the 'lipid' factor responsible for the initial lesion in atheroma. On the one hand, recent workers have suggested that all the lipid fractions of the blood are involved in the production of atheromatous plaques. The general consensus, however, still adheres to the theory that the main etiological factor is cholesterol alone and most forms of therapy are aimed at its reduction.

The recent introduction of Triparanol (Mer 29), and the substantiated claims that this is

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a specific inhibitor of excessive cholesterol biosynthesis, appeared to provide a weapon, not only for lowering the serum cholesterol but also for studying the effect of such a reduction on the other serum lipids. It was thus felt that an accurate evaluation of the role and significance of cholesterol in coronary artery disease could be determined.

At this time it seems appropriate to consider briefly our present knowledge of the biosynthesis of cholesterol. According to Cornforth,[13] acetate is the primary source of all carbon atoms of cholesterol; after activation by combination with coenzyme A, acetate condenses with itself to form acetoacetyl CoA; then follows the formation of the CoA derivative of 3-hydroxyl-3-methyl glutharic acid (HMG). There is then a reduction of one of the carboxyl groups of HMG to form mevalonic acid (MVA) and many of the factors which affect the rate of cholesterol biosynthesis act at this stage, which is ideally suited for the regulation of such biosynthesis for therapeutic purposes, although it would not prevent acetate utilization for fatty acid synthesis or ketone body formation. A long chain of reactions, however, leads to the formation of zymosterol and then desmosterol, resulting in the ultimate production of cholesterol.

According to Frantz *et al.*,[14] Mer 29-treated rats can convert lathosterol to cholesterol but are unable to convert zymosterol to cholesterol; and it was assumed that a block in the migration of the nuclear double bond from the 8,9 to the 7,8 position occurred in the steroid ring. The finding is equally consistent with a block in the reduction of the 24,25 double bond in the side chain and the accumulation of desmosterol favours this latter explanation. Steinberg *et al.*[15] have demonstrated that the inhibition of biosynthesis of cholesterol occurs just before desmosterol is converted to cholesterol and the intermediate substance formed has been isolated from the sera of animals and man treated with Mer 29.

For the purpose of this present trial it was decided to administer Triparanol (Mer 29) to a group of 11 patients, 8 of whom were suffering from coronary artery disease, 2 from hyperlipaemia and one from diabetes mellitus, complicated by diabetic retinitis. All the patients were investigated before and during treatment, which consisted of 250 mg. of Mer 29 taken each morning for 3 months.

Investigations included full clinical and ECG examinations. Biochemical estimations included evaluations of serum cholesterol, both total and beta protein-bound; serum lecithin, both total and beta-protein bound; and the electrophoresis of the alpha and beta serum lipoproteins.

The estimation of desmosterol was not carried out as a routine procedure since it was felt that the suggested method by Frantz *et al.*,[14] involving a formula using both Liebermann-Burchard and Zak reactions, was unreliable. This formula was based upon the assumption that while the Zak method gave identical colour yields with both cholesterol and desmosterol, the latter substance produced only 52% of colour development with the Liebermann-Burchard reaction. Therefore assay of the proportions of cholesterol and desmosterol can be deduced from the comparison of the higher results obtained by the Zak method with the lower results of the Liebermann-Burchard reaction. Nevertheless, considerable experience in the past with these 2 methods has shown that a much higher reading for cholesterol is given by Zak's method even in the sera of cases which have not been treated with Mer 29 and which consequently should not contain desmosterol. In fact, we would point out that while Zak's method was extensively used for the investigations published by us in 1959,[16] it was decided to revert to the more satisfactory method of Liebermann-Burchard for the next series of investigations.[17]

METHODS

1. *Cholesterol, Total.* Sackett,[18] with the slight modifications that 0.2 ml. of serum was extracted with 5 ml. of absolute alcohol and 2 ml. of ether in a 1 oz. screw-capped bottle agitated for 30 minutes on a 'Matson-type' mixer.

Drying of the alcoholic extract was carried out in a 25 ml. beaker. The dried extract was redissolved in 5 ml. of chloroform; and the Liebermann-Burchard reaction was developed in the refrigerator at 4°C. for 10 minutes.

It was felt that these modifications yielded a more accurate analysis in view of (*a*) more efficient extraction; (*b*) omission of fractional washings and (*c*) better colour development at a constant low temperature.

2. *Lecithin, Total.* The method of King.[19]

3. *Beta Protein-Bound Cholesterol and Lecithin.* Beta lipoproteins were extracted by the method of Scanu *et al.*[20] (using heparin and phenol saline) although, in view of the high level of beta lipoproteins, it was found that more efficient precipitation was obtained using only 0.5 ml. of serum with overnight refrigeration. The resultant precipitate, after centrifugation, was not resuspended in normal saline but cholesterol and lecithin estimations were carried out as above on the entire precipitate with due regard to the volume of serum originally taken. It is noteworthy that we have found that Scanu's method yields absolute separation of the beta lipoproteins, confirmed by electrophoresis, and is much superior to the method of elution from electrophoretic strips.

4. *Electrophoresis.* The EEL bath, power unit and scanner were used. The buffer solution, pH 8.6, was the barbitone-sodium barbitone buffer of Flynn,[21] modified by the addition of an equal amount of 0.05 N. sodium caprylate. 0.1 ml. of serum was applied to Whatmann 3 mm. paper and electrophoresed for 16 hours at 0.75 milliamps per strip. Strips were fixed at 110°C. for 15 minutes and then stained for 18 hours in a saturated solution of Oil Red O in 60% ethyl alcohol.

After prolonged washing in running tap water the strips were stained whilst water wet, since it was found that the routine use of hot liquid paraffin to produce transparency resulted in a removal of the stain.

Normal lipoprotein patterns were obtained from electrophoretic studies of 100 healthy females between the ages of 18-30 years, i.e. nurses, laboratory technicians, students, etc. This group was deliberately chosen because of the known freedom from atheroma.

Readings were evaluated on a 'Planimeter' and the upper limit of the normal electrophoretic scan

was taken as 100%, for both alpha and beta lipoproteins.

RESULTS

From the study of the results (Table 1) the following factors emerge:

(*a*) In most cases there was a drop in the level of the serum total cholesterol after 1 month. This, nevertheless, was followed by a rise after 3 months' treatment, but not to the pre-treatment level.

(*b*) The beta protein-bound cholesterol tended to follow the same pattern.

(*c*) There was very little alteration in the level of the serum total lecithin apart from a slight decrease in some cases.

(*d*) In the case of the protein-bound lecithin this appeared to follow the trend of the total serum lecithin.

(*e*) The alpha lipoprotein showed a general but not consistent increase.

(*f*) It would appear that there is a marked increase in the level of the beta lipoproteins and that this is produced in inverse ratio to the level of the serum total cholesterol, i.e. a lowering of the cholesterol level is accompanied by a correspondingly marked rise in the concentration of the beta lipoproteins.

TABLE 1: RESULTS

Case No.	*Diagnosis*	*Period of Treatment*	*Cholesterol (Mg. per 100 ml.)*		*Lecithin (Mg. per 100 ml.)*		*Electrophoresis*	
			Total	*Beta Bound*	*Total*	*Beta Bound*	*Alpha*	*Beta*
1.	Coronary Artery Disease	Before	270	180	260	160	56%	88%
		1 month	265	142	300	160	56%	129%
		3 months	250	190	260	160	80%	121%
2.	Coronary Artery Disease	Before	260	152	263	160	33%	73%
		1 month	180	148	225	140	60%	71%
		3 months	245	188	225	190	67%	65%
3.	Coronary Artery Disease	Before	350	260	300	222	26%	106%
		1 month	280	230	270	200	30%	120%
		3 months	220	150	190	150	31%	130%
4.	Coronary Artery Disease	Before	200	106	230	150	47%	94%
		1 month	200	128	230	140	56%	121%
		3 months	180	112	250	150	67%	132%
5.	Coronary Artery Disease	Before	305	200	300	195	60%	115%
		1 month	245	120	220	160	33%	103%
		3 months	270	146	250	170	33%	109%
6.	Coronary Artery Disease	Before	185	122	200	115	67%	82%
		1 month	150	86	180	105	56%	91%
		3 months	190	124	190	130	33%	65%
7.	Coronary Artery Disease	Before	250	130	225	130	56%	91%
		1 month	180	80	200	95	60%	132%
		3 months	180	100	225	120	65%	123%
8.	Coronary Artery Disease	Before	335	200	275	175	47%	118%
		1 month	245	200	250	180	67%	126%
		3 months	230	184	240	160	80%	109%
9.	Hyperlipaemia	Before	335	280	315	280	67%	159%
		1 month	470	290	450	300	60%	170%
		3 months	310	250	320	270	61%	179%
10.	Hyperlipaemia	Before	490	400	480	380	27%	170%
		1 month	410	350	430	360	27%	250%
		3 months	280	165	315	190	47%	180%
11.	Diabetes Mellitus ..	Before	360	154	330	155	85%	123%
		1 month	190	90	250	170	80%	132%
		3 months	225	116	260	175	67%	103%

DISCUSSION

That the etiology of coronary artery disease remains obscure is evident from the current 2 main forms of treatment which are directed at (1) anticoagulant therapy, and (2) a reduction in the serum cholesterol.

It is felt that both forms of therapy are empirical and result from theories which have not, to date, been substantiated by full scientific investigation.

Anticoagulant therapy has been demonstrated by numerous workers to be both dangerous and inefficacious. This is not surprising since many investigators have shown that coronary artery disease is mainly due to coronary occlusion resulting from lipid deposition, rather than from thrombosis. It is, however, appreciated that the presence of a thrombus superimposed upon an atheromatous plaque cannot be neglected.

The significance of the level of the total serum cholesterol would appear to have assumed undue importance because of the comparative ease of its estimation over that of the other serum 'lipids.' It must be pointed out that these analyses are subject, not only to variations due to technical errors, but also to physiological fluctuations throughout the day. Hence slight alterations may quite conceivably be due to one or both of the above factors, although many workers have attached great importance to such minutiae. For instance, Kingsbury *et al.*[22] in a recent article investigating changes in serum cholesterol following the administration of cod liver oil, noted a decrease of 8 mg. in one patient. We feel that this trivial reduction falls easily within the limits of technical error or physiological variation.

Numerous animal experiments involving the feeding of large doses of cholesterol have resulted in the production of atheroma, but the experimental animals, mainly rabbits, have been strictly herbivorous and their metabolism is in no way equipped to deal with what is to them an entirely foreign substance.

Therefore the ease of estimation of cholesterol, the results of animal experiments, the finding of cholesterol crystals in atheromatous plaques, and the high levels of cholesterol associated with coronary occlusion have most strongly suggested that this substance is a vital, if not the most important, etiological factor associated with coronary artery disease. Thus reduction of serum cholesterol has been attempted by various means.

While a reduction of dietary fat is apparently logical, the readiness with which cholesterol is synthesized in the body from acetate mitigates against any attempt to maintain a low lipid concentration.

The administration of large doses of nicotinic acid does produce a marked reduction of serum cholesterol although many side effects are experienced and Rivin[23] has noted that such patients have developed jaundice consequent upon fatty infiltration of the liver. Peters and Van Slyke[24] state that nicotinic acid causes the diversion of methyl groups from choline to creatine and trigolline, leading to such fatty degeneration.

With the introduction of Triparanol (Mer 29) we have at last been provided with a drug which will reduce serum cholesterol safely and efficiently. Much useful work has been carried out on the cholesterol-reducing quality of this and other forms of therapy but little, if any, attention has been directed to the effect of such cholesterol reduction on the levels of the other serum 'lipids.' Thus the feeding of unsaturated fatty acids such as corn oil, cod liver oil, sun flower seed oil and fatty acid preparations, i.e. Lipostabil, have been regarded as satisfactory when judged entirely by the subsequent reduction of cholesterol levels.

However, recent work by Bottcher *et al.*,[9] who analysed the lipid concentration in atheromatous human aortas, has shown a concentration of unsaturated fatty acids up to 50% and it would appear that these substances are as important in the etiology of coronary artery disease as is cholesterol. It is felt that there is little if any chemical difference in the structure of animal or vegetable fatty acids and no appreciable benefit can be gained from the substitution of one type of fatty acid for another. Patients placed on these vegetable fatty acids show either an increased lipoprotein pattern or this remains *in statu quo ante*.

With regard to the use of Triparanol (Mer 29), all cases have shown a marked increase in the level of the beta lipoproteins, although this has been accompanied by a definite reduction in the serum cholesterol. Nevertheless, with the lowering of serum cholesterol there is a corresponding rise in the concentration of desmosterol (Frantz *et al.*[14]), and this substance may be in itself an atherogenic factor and capable of producing esters with fatty acids. As noted earlier, the estimation of desmosterol was not carried out because the suggested technique appeared to be basically unsound.

Kayahan[12] has demonstrated an increased and pathological affinity of the beta proteins for lipids and, while we have been unable to reproduce this work, from our subjective work[25]

it would appear that the main etiological factor in atheroma consists of an increased carriage of lipds by a normal concentration of beta proteins. The consequent supersaturation ' facilitates a ready deposition of lipid upon the arterial wall. The overloading of lipids may have some effect on the blood coagulation factors found in the beta proteins. Both Greig,[26] and ourselves,[16] have noted that the increased lipid concentration inhibits the action of plasmin, while Fullerton *et al.*[27] have observed a shortening of the coagulation time after the ingestion of a fatty meal.

The importance of the role of the beta lipoproteins in atheroma has been recently confirmed by the work of Gero *et al.*[28] on the anti-atherogenic effect of cross-species immunization with beta lipoproteins in cholesterol-fed animals.

We would suggest that too much emphasis has been placed on the role of cholesterol in the production of atheroma. The specific lowering action of Triparanol (Mer 29) has been accompanied by a marked increase of lipids carried by the beta proteins. It would appear that cholesterol, by its ability to form esters, may produce a restraining effect on the carriage of fats by the beta proteins and its role, in atheroma, may be of a passive or even beneficial, nature.

Clinically, there has been no improvement consequent upon the reduction of the level of the total serum cholesterol by Triparanol (Mer 29) and the accompanying rise in the beta lipoproteins would indicate that this drug may, in fact, increase the risk of the development of atheroma. It cannot be too strongly emphasized that cholesterol-reducing drugs may be a potential danger in the treatment of atheroma and, while Triparanol (Mer 29) meets the claims of its manufacturers (as regards its chemical action) its use would appear to have been advocated by a misconception of the true etiology of coronary artery disease.

The many hundreds of investigations we have carried out, supported by clinical and ECG findings, have demonstrated that the most reliable screening test for coronary artery disease is that of the electrophoresis of the lipoproteins, using stains such as Oil Red O, which indicates the presence of lipids other than cholesterol. It is apparent that research should be directed towards the abnormal affinity of the beta proteins for lipids and to the production of therapeutic substances which will lower, by competition, the level of the lipids so carried.

' When the unclean spirit has gone out of a man, he roams through waterless places in search of a resting place; finding none he says, " I will return to my house which I left." And when he has come, he finds the place swept and then he goes and takes seven other spirits more evil than himself, and they enter in and dwell there; and the last state of that man becomes worse than the first.' (Luke 11).

SUMMARY

1. Eleven patients, 8 suffering from coronary artery disease, 2 from hyperlipaemia, and one from diabetic retinitis, were treated (over a period of 3 months) with Triparanol (Mer 29).

2. Whilst no clinical improvement was observed, chemically it was seen that the reduction in the total cholesterol was accompanied by a marked rise in the level of the beta lipoproteins.

3. The doubtful role of cholesterol as an etiological factor in atheroma is discussed.

4. The danger of cholesterol-lowering substances is stressed.

We wish to thank the Wm. S. Merrell Co., Cincinnati, U.S.A., for the supply of Triparanol (Mer 29).

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AORTITIS: A REVIEW

WITH A FURTHER CASE REPORT OF AN IDIOPATHIC TYPE IN AN AFRICAN CHILD

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Several cases have been encountered in this hospital of an idiopathic aortitis in young Bantu children.[1, 2] The ages ranged from 7 to 16 years. There were 2 males and 4 females. Five cases were hypertensive due to renal artery occlusion, and in the sixth hypertension confined to the upper part of the body was due to thrombosis of the thoracic aorta. The clinical and serological findings excluded syphilis and there was also no evidence that rheumatic fever, rheumatoid arthritis or tuberculosis played any part in the aetiology. The pathological findings were not unlike 'pulseless disease,' although in several cases the arch of the aorta was not affected. The young age of most of the subjects did not favour a diagnosis of giant-cell arteritis. It was concluded that clinically and pathologically the disease was probably either an atypical manifestation of 'pulseless disease' or 'giant-cell arteritis' in the very young.

The following is a report of a further case of idiopathic aortitis presenting interesting clinical and pathological features somewhat different from those reported in the previous cases.

CASE HISTORY

A female Bantu child aged 4 years was admitted to hospital on 28 December 1959. A week before admission this child, who had always been in perfect health, developed swelling of the whole body, more marked in the legs. At the same time she was noted to be increasingly breathless on exertion until the day before admission to hospital, when she was dyspnoeic at rest. She could sleep only when propped up with pillows.

Examination revealed a child propped up on 4 pillows, dyspnoeic at rest, and with gross generalized oedema. The jugular veins were engorged up to the angles of the jaw. All the pulses were palpable but those in the legs were much weaker and lagged behind the radial pulses. The blood pressure in the arms was 120/100 mm. Hg, while that in the legs was 100 mm. Hg systolic, obtained by the flush method.

The heart was enlarged into the 6th intercostal space in the mid-axillary line with an apical heave suggestive of left ventricular hypertrophy. A protodiastolic gallop rhythm

was audible at the apex of the heart. The liver was palpable 3 fingers below the costal margin. The rest of the examination was negative.

LABORATORY INVESTIGATIONS

The urine showed the presence of albumin ++. Microscopic examination of an unspun specimen under low power magnification, showed 10 erythrocytes and 40 polymorphonuclear leucocytes with occasional granular and hyaline casts.

The blood urea was 16 mg. per 100 c.c., the total blood cholesterol was 132 mg. per 100 c.c. The haemoglobin was 15.5 g. %. The total leucocyte count was 8,400 per c.mm.

The blood Wassermann reaction was negative and there was a negative reaction to an intradermal injection of purified protein derivative of tuberculin.

The clinical diagnosis was coarctation of the aorta with congestive cardiac failure.

During the first 12 hours the child was given 0.5 mg. of digoxin by mouth followed by 2 further doses of 0.25 mg. at 8-hourly intervals. She was maintained on 0.25 mg. given once a day. In addition 250,000 units of penicillin were given intramuscularly every 8 hours.

An X-ray of the chest showed cardiomegaly with a cardio-thoracic ratio of 65%. The lung fields were clear. An electrocardiogram showed marked left ventricular hypertrophy.

The following day the venous pressure had subsided, the gallop rhythm had disappeared, but the child was still oedematous.

Three days after admission the patient developed a grand mal seizure. The pulse rate was 190 beats per minute, the blood pressure in the arms was 150/80 mm. Hg, while that in the legs was 100 mm. Hg systolic by the flush method. The jugular venous engorgement was once more up to the angles of the jaw and the liver was palpable 3 fingers below the costal margin. The protodiastolic gallop rhythm was again audible.

Cerebrospinal fluid obtained by lumbar puncture showed 2 polymorphonuclear leucocytes and 2 lymphocytes per c.mm. The total protein was 92 mg. per 100 c.c., the sugar was 120 mg. per 100 c.c. and the chlorides (as sodium chloride) were 760 mg. per 100 c.c.

The child was given an intramuscular injection of 1 c.c. of paraldehyde and placed in an oxygen tent. This appeared to control the initial seizure, but over the next 8 days there were 4 further grand mal attacks. The blood pressure in the arms after the last fit had risen to 185/100 mm. Hg, but remained at 100 mm. Hg in the legs. The blood pressure was then measured every 2 hours and the patient received 0.9 mg. of Serpasil by intramuscular injection whenever the blood pressure rose above 120 mm. Hg. systolic.

Despite all treatment the signs of congestive cardiac failure increased over the next 3 weeks and the child died 36 days after admission.

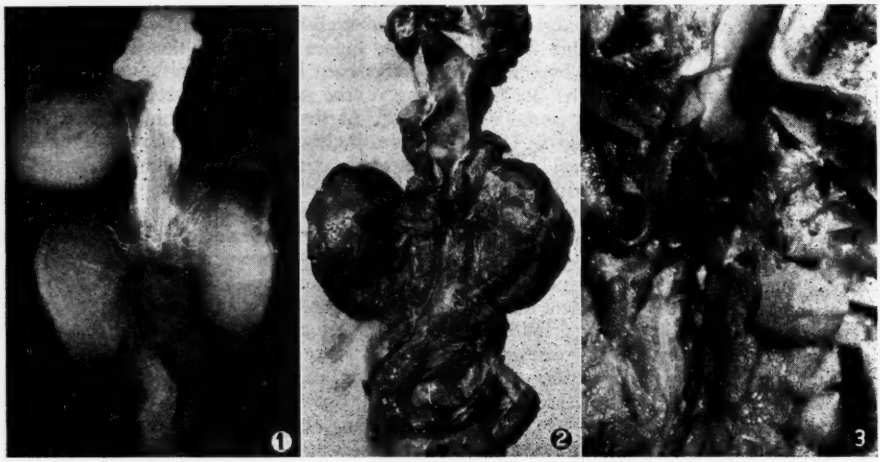

Fig. 1. Post-mortem radiograph taken after injection of an opaque medium into the aorta. Note the hold-up of the dye proximal to the renal arteries.
Fig 2. Opened aorta showed narrowing below origin of the coeliac artery.
Fig. 3. Close-up view of narrowed aorta.

AUTOPSY FINDINGS

There was mild oedema of the legs and sacrum. The right *pleural* cavity and the *peritoneal* cavity contained 1 pint and 2 pints of straw-coloured fluid respectively.

The significant findings were confined to the cardiovascular system. The *heart* (170 g.) showed marked left ventricular hypertrophy and moderate right ventricular hypertrophy. The valves were normal. The coronary arteries were patent. Barium injection studies of the aorta showed a block immediately proximal to the origin of the renal arteries (Fig. 1). The intima of the ascending aorta, arch and thoracic portions was normal. The carotid and subclavian arteries appeared healthy.

A fairly recent thrombus completely occluded the abdominal aorta immediately distal to the origin of the mesenteric arteries. Distal to this point the lumen of the aorta was considerably narrowed and the wall markedly thickened (Figs. 2, 3). The narrowing extended to the bifurcation and also involved the common iliac arteries.

The renal arteries were almost completely occluded by recent and old thrombi. Beyond the narrowing of the iliac arteries there were recent ante-mortem thrombi which extended to the commencement of the popliteal artery on the right side and to the femoral artery on the left.

The remaining organs showed passive congestion. There were no enlarged lymph nodes and the spleen was normal.

Microscopic examination of the *heart* showed hypertrophy of the muscle fibres with occasional foci of interstitial fibrosis. The arch of the aorta, thoracic aorta, coeliac, common carotid and subclavian arteries were normal.

Sections of the abdominal aorta immediately proximal to the origin of the renal arteries showed the vessel to be of normal diameter.

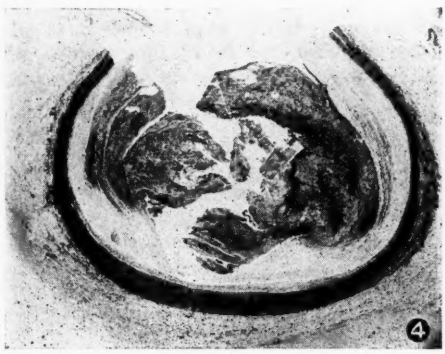

Fig. 4. Section of aorta proximal to the hypoplastic segment showing a thrombus almost completely occluding the lumen. Note the thickened intima. (Elastic-Masson ×3.7. Original magnification: ×7.)

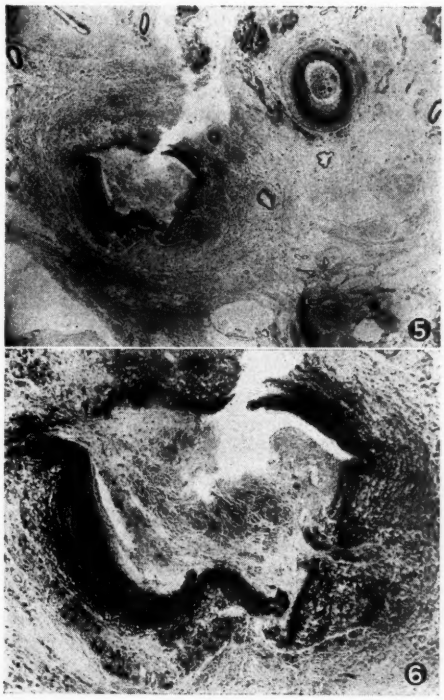

Fig. 5. Section of aorta through hypoplastic segment. Note the marked narrowing (compare with Fig. 4).
There is a thrombosed ovarian artery with a thickened intima at top right (Elastic-Masson: ×3.7. Original magnification: ×7.)

Fig. 6. Higher magnification of hypoplastic segment. Note the fragmentation of the elastic (Elastic-Masson: ×15.8. Original magnification: ×30).

The lumen was, however, markedly narrowed by both old, fibrous intimal thickening and recent ante-mortem thrombus (Fig. 4). The adventitia was also markedly fibrosed and showed heavy focal infiltration by plasma cells and lymphocytes with capillary proliferation. In some areas the inflammatory cells extended into the media of the aorta for a short distance and here the elastic was fragmented and frayed. Immediately distal to the origin of the renal arteries the actual diameter of the aorta

narrowed remarkably. This was quite independent of the occlusion produced by the intimal thrombosis. There appeared, in effect, to be a true hypoplasia of the aorta at this level plus a thrombotic narrowing (Fig. 5).

The elastic of the media in this area showed fragmentation and necrosis and the intima was markedly thickened. In addition, the elastic was clearly visible with the ordinary haematoxylin-eosin stain, being intensely basophilic. In parts the entire wall of the aorta appeared to have disintegrated and to have become incorporated in the thrombus (Fig. 6). The entire wall was heavily infiltrated by chronic inflammatory cells and many of the vasa vasorum showed a marked endarteritis (Figs. 7-9).

The *ovarian* artery was also occluded by old thrombus.

The *para-aortic lymph nodes* showed an interesting picture. There was marked sinus reaction with progression to fibrosis of the sinusoidal spaces and plasma cell infiltration. Several lymph nodes showed foci of necrosis with epithelioid cells and Langhans type giant cells, a picture highly suggestive of tuberculosis (Fig. 10). Acid-fast bacilli were, however, not observed and there was no evidence of tuberculosis elsewhere in the body. In one lymph node there were deposits of amyloid-like material.

The narrowing of the aorta with the associated severe inflammatory changes extended down to the bifurcation. At this point, although occluded by thrombus, the common iliac arteries were of normal diameter.

The *left and right renal arteries* were partially occluded by recent and old thrombus and also showed a dense infiltrate of plasma cells in adventitia and media.

The *left kidney* showed foci of hyalinization of glomeruli and slight lymphocytic infiltration

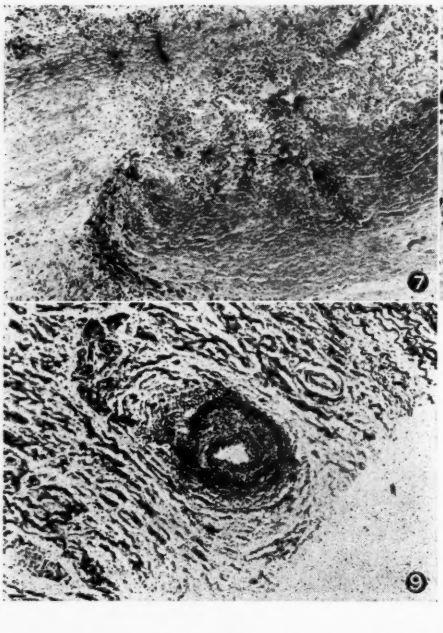

Fig. 7. Inflammatory changes in the media of the aorta. (Haematoxylin and eosin: × 55. Original magnification: × 120.)

Fig 8. Higher magnification of Fig. 7. There are numerous plasma cells and lymphocytes associated with fibrolastic proliferation. (Haematoxylin and eosin: × 220. Original magnification: × 480.)

Fig. 9. Endarteritis of the vasa vasorum. (Elastic-Masson: × 55. Original magnification × 120.)

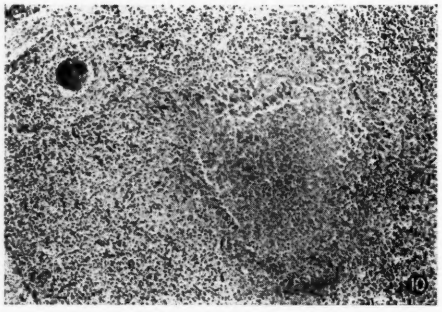

Fig. 10. Section of a para-aortic lymph node showing a granuloma with necrosis of the centre and a single giant cell. (Haematoxylin and eosin: × 55. Original magnification: × 120.)

of the interstitial tissue. Several tubules contained hyaline casts. The vessels were normal. The *right kidney* was normal histologically.

As no specific aetiological factor has as yet been discovered in any of the cases of idiopathic aortitis, the possible causes of aortic arteritis will be reviewed.

SYPHILIS

The lesions of syphilitic aortitis are too well known to warrant detailed repetition. Suffice it to recall that the aortic lesions are essentially an affection of the vasa vasorum, spreading from adventitia to media. The arch of the aorta is by far the commonest site of syphilitic lesions, the arch immediately above the aortic valve being involved first. As a rule the lesions cease at the level of the diaphragm. Histologically, the earliest change is a perivascular cellular infiltration associated with periarteritis and endarteritis of the small vessels in the adventitia. The inflammation extends into the media, producing destruction of the elastic and muscle tissue followed by a replacement fibrosis. Fibrous thickening of the intima develops. Congenital cardiovascular syphilis is extremely rare.[3] The clinical and pathological manifestations of cardiovascular syphilis usually become manifest between 35 and 66 years of age. The average time between the primary infection and the commencement of symptoms of aortitis is approximately 2 years.

RHEUMATIC FEVER

There is no doubt that in some cases of rheumatic fever an aortitis may occur.[4-6] Grossly, the lesions have been described as nodular fibrous thickenings,[7] elevated almost transparent plaques and ridges of brownish colour,[4] soft flat glassy cushions,[8] and yellow, elevated nodules and streaks.[9]

Microscopically there may occur bands of non-nucleated fibrillar material in the intima, bordered by rows of basophilic cells. The muscle of the media may be degenerate and the elastic fragmented, while the vasa vasorum may show swelling of the endothelial cells with a perivascular lymphocytic infiltrate. Occasionally Aschoff bodies are seen in the adventitia and the collagen of the adventitia and the media may be swollen.[10]

According to Klotz,[7] the area of predilection in rheumatic aortitis is the ascending limb. Rarely the arteritis may be so severe as to cause various forms of ectasia and sacculation.

Pappenheimer and Von Glahn[5] pointed out that the aortic lesions are not merely extensions of the lesions seen in the aortic valve, since they may occur at a distance from the valve. Klinge[8] claimed that although the lesions are more numerous in the ascending and thoracic portion, any part of the aorta may be involved, and felt that aortic involvement is the rule rather than the exception.

Gray and Aitken[11] described in detail the late gross lesions in the aorta and pulmonary artery. These lesions consisted essentially in scarring of the media and thickening of the intima. Gould[12] described foci of fibrinoid degeneration of the veins and arteries of the adventitia in the acute stage. Pappenheimer and Von Glahn[4] claimed that the chronic lesions can be distinguished from those of syphilis in that the latter are not restricted to the neighbourhood of nutrient vessels and are accompanied by the production of vascular granulation tissue and gummatous necrosis.

RHEUMATOID ARTHRITIS

Several authors have described an aortitis occurring in rheumatoid arthritis.[13, 14] Pirani and Bennett[15] found irregular outpouchings of the aorta in the region of the sinuses, with some wrinkling of the intima.

Microscopically, sections of the aorta near the aortic valve disclosed a marked infiltration with lymphocytes and plasma cells, especially around the vasa vasorum, with fibrosis of all layers and narrowing of the lumina of the vasa vasorum. The incidence is not confined to adults. Bennett[16] reported the case of a young boy who developed progressive rheumatoid arthritis at less than 3 years of age and at the time of his death at 8 years was crippled and deformed and had a marked aortitis with early aneurysm formation. The histological changes were indistinguishable from those of syphilitic aortitis, but serological studies had been negative and there was no clinical evidence of syphilis.

A further microscopic feature is the presence of granulomatous lesions resembling the typical rheumatoid nodule.[17, 18] Mallory[19] described focal necrosis of the media of the root of the aorta, fibrous intimal thickening, vascularization of the media with destruction of muscle and elastic, and perivascular cuffing of the vasa vasorum. Shilder *et al.*[20] found calcium deposits in the intima. Clark *et al.*[21] described lesions of the root of the aorta showing elastic and muscle destruction of the media

with replacement by granulation tissue, intimal fibrous thickening and adventitial fibrosis with lymphocytic infiltration. Fibromuscular thickening of the walls of the vasa vasorum was a feature.

Lomas *et al.*[22] reported the findings in a 7½-year-old Negro girl with rheumatoid arthritis who also showed a markedly raised blood pressure in the arms and an enlarged heart. At autopsy there was segmental mural thickening of the aorta from 2 cm. beyond the aortic valve to the level of the renal arteries. There was also moderate narrowing of the left common carotid, left subclavian and inferior mesenteric arteries.

Histologically there was intimal thickening, destruction of the elastic of the media with granulation tissue proliferation, adventitial fibrosis and endarteritis of the vasa vasorum.

Aortic lesions similar to those seen in rheumatoid arthritis have also been described in the related disease of ankylosing spondylitis.[23]

TAKAYASHU'S DISEASE (PULSELESS DISEASE)

This strange disease was described by Takayashu[24] in 1908 although the earliest reported case was probably that by Savory[25] in 1856. Since then numerous reports have appeared in the literature and the subject has been well-reviewed.[26, 27]

Clinically the disease generally occurs in young women and is associated with cerebral, ocular and upper extremity symptoms. The most characteristic vascular sign is absence of arterial pulsation in the neck, head and arms.

Pathologically, the primary lesion consists of an acute, phlegmonous arteritis with adventitial thickening and an infiltrate of lymphocytes, monocytes and polymorphs invading the entire wall. Where the cellular infiltrate reaches the media and intima, intra-arterial thrombosis may be precipitated.

In nearly all cases the process has been a segmental one involving the arch of the aorta and the great vessels arising from the arch. Occasionally the thoracic aorta may be involved but then only in its proximal part. Ask-Upmark,[28] however, reported a case in a 40-year-old female with renal atrophy, apparently due to extension of the disease to the renal vessels, and Barker and Edwards[29] described a case in which there was involvement of the entire thoracic aorta. Reader and Harbitz[30] reported a case with narrowing of the renal arteries at their origin. Correa and Araujo[31] described the disease in a 15-year-old girl with involvement of the ascending aorta, the arch, descending aorta and left common carotid artery. In Oota's patient[32] there was extension of the lesions to the abdominal aorta, the mesenteric arteries and also to the pulmonary arteries. Harbitz[33] found involvement of the arch and descending aorta, as well as the great vessels arising from the arch. Koszewski and Hubbard[27] stressed the virtual restriction of the arteritis to the original branchial branches, even to the extent of suggesting the term congenital branchial arteritis.

Giant cells are not generally a histological feature, although Frovig and Löken's case[34] showed numerous giant cells in the media. Several authors point out that the importance of the latter should not be over-estimated as giant cells are a common finding in atrophy of muscular or elastic tissue.[35]

The distinction from temporal or giant cell arteritis is not clear-cut, and histologically they are similar in many respects.[28] Temporal arteritis tends to occur in elderly patients who usually show only involvement of the temporal arteries, although this is not invariable.

Kalmansohn and Kalmansohn[36] favoured the term thrombo-angiitis obliterans of the branches of the aortic arch because of the consistent demonstration of intravascular clot formation with inflammation of the vessel wall, and because of the peculiar anatomic localization (aortic arch).

The aetiology of the disease remains obscure. Ask-Upmark[28] suggested a rheumatic or rheumatoid origin. This is supported by Birke *et al.*,[37] who reported a clinical analysis of 10 cases. One subject had what they termed a 'rheumatic systemic disease (collagenosis),' and they interpreted the aortitis as a rheumatic brachiocephalic arteritis. Three of their cases had raised antistreptolysin 0 titres. One case also had tuberculous cervical adenitis, and they suggested that tuberculosis might be a precipitating factor in the development of the arteritis in some instances. Misra *et al.*[38] tended to support the latter view. McCormick and Neuberger[39] suggested that the disease may be an allergic arteritis, and could be grouped together with endarteritis obliterans, periarteritis nodosa, and giant cell arteritis.

TEMPORAL OR GIANT CELL ARTERITIS

This condition was first described by Horton *et al.*[41]. They reported on 2 elderly patients complaining of soreness of the scalp with painful nodules along the temporal arteries.

Pathologically, the latter showed granulation tissue in the adventitia, perivascular round cell infiltration of the vasa vasorum, and slight cellular infiltrate and haemorrhage in the media. The intima was thickened, and the lumen occluded in places by recent thrombus.

Many authors have since described involvement of arteries other than the temporal. Cooke *et al.*[42] reported 7 cases aged 66 to 73 years, 6 of whom had symptoms suggesting generalized arterial disease, and this was confirmed by autopsy in 2 cases. In the autopsied cases changes were seen in the aorta, temporal, radial, subclavian, femoral, coronary, renal, retinal, coeliac and mesenteric arteries. The femoral vein was involved in one case.

They stressed that in most of the reported cases generalized symptoms preceded the temporal artery thrombosis, such as muscle aches, joint pains, fever, night sweats, lassitude and weight loss. Headache, vomiting and papilloedema were prominent features, and vision was often impaired. The media contained foci of chronic inflammatory granulation tissue infiltrated by lymphocytes, plasma cells and mononuclears, with occasional giant cells. The intima often showed hypertrophy with reduplication of the elastic lamina, and thrombosis was a common sequel. They considered that the lesion probably began as a periarteritis in a small segment of a vessel and, with continuation of the process, spread to the media and intima.

Gilmour[43] described 4 cases and introduced the term giant cell chronic arteritis. In his subjects the disease chiefly affected the aorta and the branches of its arch. In reviewing the literature he found that the temporal arteries were affected in 18 cases, the aorta in 6, the internal carotids in 4, common carotids and iliacs in 3, the subclavian and external carotids in 2, and the innominate, coronary and occipital arteries in 1 case each.

He claimed that the inflammatory process started in the media and extended into the adventitia. Nevertheless all his illustrations showed adventitial inflammation and one has to agree with Cooke *et al.*[42] that the inflammation commences in the adventitia. Gilmour[43] described infiltration of the media by lymphocytes, plasma cells and occasional polymorphs, followed by capillary invasion, fibroblastic proliferation and collagen formation, with multinucleated giant cells in scanty numbers. The infiltrating cells replaced the muscle and separated the elastic. The adventitia was thickened and fibrotic and infiltrated focally with lymphocytes and plasma cells. The intima was always thickened.

The most important effects were thromboses of stenosed vessels in which cerebral infarction occurred. The patients' ages were 23 years (female), 59 years (female), 63 years (male), and 64 years (female).

Reid[44] described 4 cases of giant cell arteritis of the aorta, and introduced the term granulomatous aortitis. He found infiltration of the media by plasma cells, lymphocytes and mononuclears. Giant cells were usually present, and the muscle and elastic was destroyed. In older cases the adventitia was sclerotic. Some of the vasa vasorum showed an endarteritis. He pointed out that the particular liability of the aorta to be affected in this disease is shown by the observation that, in every reported case where the aorta had been adequately examined microscopically, characteristic changes have been found. These cases, together with those of aortitis without cranial arteritis, have been enumerated by Cardell and Hanley.[45]

In general the disease is one of elderly people. At one time it was felt that women were affected more frequently than men, but Harrison,[46] in an excellent review, stated that there is probably no real sex bias.

Gelfand[47] reported a case in an African child of 2 years who, at autopsy, showed fusiform dilatation of the ascending aorta and arch. There was scarring of the intima of the aorta extending to just distal to the origin of the superior mesenteric artery.

Heptinstall *et al.*[48] described giant cell arteritis affecting the aorta in 2 cases. Other authors have also described aortic lesions in this disease.[49, 50]

The aetiology of this disease remains obscure. Although no specific organism has ever been isolated, Harrison[46] supported an infective basis, and quoted several cases from the literature which were preceded by an infection. McCormick and Neuberger[39] pointed out that, although giant cell arteritis and pulseless disease may differ clinically, the occasional overlapping of signs and symptoms is not surprising when one considers the possible sites of both conditions. They showed that the pathologic manifestations are certainly very similar, if not identical, and suggested that conditions like periarteritis nodosa, endarteritis obliterans, giant cells arteritis, and 'pulseless disease' belong in the group of allergic arteritis. Certainly all these diseases have features in common, especially fibrosis of the intima and granulomatous foci, features des-

cribed by Berblinger[51] as occurring in most cases of allergic arteritis.

The possibility that rheumatic disease may be an aetiological factor has also been suggested. The case reported by Paviot *et al.*[52] also had active rheumatic carditis at the time, and both this and the arteritis responded dramatically to salicylates. Both of Sjövall and Windblad's cases[53] developed crippling arthritis. Kimmelstiel *et al.*[54] believed that giant cell arteritis might have its origin in a peculiar lesion of elastic membrane.

TUBERCULOSIS

It is generally accepted that tuberculous involvement of the aorta is secondary to either pulmonary tuberculosis or tuberculosis of the peri-aortic lymph glands.[3] Rarely aneurysm formation may result.[55] Thieme *et al.*,[56] however, described a case of what they thought was primary tuberculous peripheral vascular disease in a male of 35 years. This patient presented with peripheral vascular deficiency, which necessitated amputation of several digits.

Histological examination of biopsies from ulcerated areas showed 'obliterating tuberculous endophlebitis and phlebitis,' with granulation tissue filling the lumen of the veins, in which there were nodular formations of epithelioid cells and giant cells, with caseous necrosis. Tubercle bacilli were not observed microscopically, nor was there any systemic evidence of tuberculosis.

While not denying completely the possible occurrence of primary tuberculous aortitis, we think it seems highly unlikely that the tubercle bacilli could localize in the wall of the blood vessel, producing severe changes, without a tuberculous focus elsewhere in the body. Certainly in this hospital where tuberculosis is very frequent one has never encountered 'primary tuberculous arteritis,' although secondary involvement of blood vessels, generally due to extension from an adjacent lymph node, is seen occasionally.

MISCELLANEOUS

There are a few other extremely rare causes of aortic arteritis. Periarteritis nodosa has been reported to affect the aorta, but in this disease the smaller vessels are mainly affected and there is striking fibrinoid necrosis. The 'controversial' Buerger's disease shows venous as well as arterial involvement.

DISCUSSION

In a previous communication[2] the possible pathogenesis and aetiology of idiopathic aortitis was discussed. It was suggested that the disease was probably related to 'pulseless disease' and giant cell arteritis. No infective agent was demonstrated, but the possibility of a viral aetiology was not excluded. Toxins were also considered as a possible aetiological factor.

The case reported here presents several interesting features. There was undoubtedly hypoplasia of the abdominal aorta below the origin of the renal arteries. In addition there was marked inflammation of the wall of the aorta with superimposed thrombosis, findings not generally associated with hypoplasia *per se*. There was thus an aortic arteritis as well as aortic hypoplasia, the hypoplastic vessel possibly having been rendered more susceptible to the arteritis by virtue of its developmental abnormality.

The findings in the para-aortic lymph nodes are of interest, although the part they played in the aortitis is obscure. Although acid-fast bacilli were not observed, the histological features were suggestive of tuberculosis. The latter disease is very frequent in this hospital and the allergic manifestations with a heightened sensitivity response are often seen. Massive caseous necrosis is a frequent autopsy finding, even in the presence of a very few bacilli. The appearances in the lymph node may have represented a hypersensitivity response to tuberculosis or some other allergen such as histoplasmosis, the resultant perivascular inflammatory changes producing an endarteritis of the vasa vasorum. The ischaemia so produced could have resulted in the necrosis and destruction of the media of the aorta.

As with most of the previously described cases of idiopathic aortitis, hypertension due to renal artery occlusion was a prominent feature. There is no doubt that the renal artery thrombosis was secondary to spread of the arteritis from adventitia through to intima.

Future cases should be actively investigated in an attempt to uncover an aetiological factor. Every subject should be tuberculin-tested and laboratory investigations to exclude an autoimmune basis for the disease should be pursued.

We would like to thank the Director of the South African Institute for Medical Research for facilities granted and the Superintendent for permission to submit this paper for publication.

Mr. M. Ulrich, of the Photographic Department of the South African Institute for Medical Research, produced the photographs.

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NOTES AND NEWS : BERIGTE

Dr. D. J. Jacobs, M.B., B.Ch., D.O. and Dr. R. van Zinderen Bakker, M.B., Ch.B., M. Med. Ophth., have commenced practice in partnership at 41 van Riebeeck Medical Building, Schoeman Street, Pretoria. (*Telephones*: 2-3443; 2-4156).

* * *

Dr. Aaron Penn, M.B., B.Ch., M.R.C.O.G., has joined Dr. Bernard Berger, M.R.C.O.G., in obstetrical and gynaecological practice at 712 Harley Chambers, Jeppe Street, Johannesburg. (*Telephone*: 22-3348).

The Natal Pathological Laboratory (*Pathologists*: Drs. Norman H. and Lindsay H. Walker) will move to new premises in Suite 711 (7th Floor) West Walk, 405 West Street, Durban.

The laboratory (which is privately owned) was opened in 1921 by Dr. N. H. Walker and has been in its present premises Chancery Bldgs., Smith Street, Durban, since 1926.

The opening date in West Walk is 18 December 1961.

THE MAURICE WEINBREN AWARD IN RADIOLOGY

1. This Award consists of a Certificate and a prize to the value of R 50.00.

2. It will be made annually (in respect of a calendar year) for a published paper of sufficient merit dealing either with radiodiagnosis or radiotherapy.

3. The Award is restricted to medical practitioners registered in South Africa, but the paper may have appeared in any medical journal published in South Africa, or in the *British Journal of Radiology* or the *Journal of the Faculty of Radiologists*, London.

4. The Selection Committee may change or add to the names of the journals in which candidates may have published papers submitted for consideration.

5. Authors who wish to be considered for this Award must advise the Honorary Secretary of the Selection Committee to this effect by 31 December each year.

6. They must provide 6 copies of the paper submitted for consideration not later than the end of February in the succeeding year.

7. The address of the Acting Honorary Secretary of the Selection Committee is:

Dr. H. A. Shapiro,
P.O. Box 1010,
Johannesburg.

8. Members of the Selection Committee are not eligible for the Award.

9. The decision of the Selection Committee, in connexion with the making of an Award, is final and binding.

* * *

MEDICAL COUNCIL BYE-ELECTION

Dr. E. W. Turton was the successful candidate in the recent bye-election for an elected member of the Medical Council. The result of the poll was as follows:

Frack, I.	601;
Freed, L. F.	251;
Le Roux, J. J. du Pre	796;
Turton, E. W.	1032;
Schneider, T.	519.

Dr. Turton's membership of the Council is for the balance of the quinquennial period of the life of the present Council, i.e. until 31 December 1963.

* * *

R 200,000 GRANT FOR ANAEMIA RESEARCH

WELLCOME TRUST'S AID FOR TROPICS

The Wellcome Foundation has made available R 200,000 to help integrated research by several groups into severe anaemias prevalent in tropical countries—special reference being given to the malabsorption syndrome and tropical sprue.

The Wellcome Foundation trustees state that further research into the causes of anaemia is urgently needed. In many cases there is great difference between anaemias occurring in tropical countries and those prevalent in climatically temperate areas. In making the grant the Foundation will be materially assisting this field of medical research.

The Foundation already supports work by Dr. Henry Foy and Dr. Athena Kondi (who are studying tropical anaemias caused by malaria, hookworm and other causes, at the Medical Research Laboratories in Nairobi, Kenya) and by Dr. Selwyn Baker and others, who are investigating the malabsorption syndrome in the Wellcome Sprue Research Unit at the Christian Medical College, Vellore, South India.

NEW LABORATORY

Included in the allocation of R 200,000 is the sum of R 90,000 to build and equip the Wellcome Laboratory of Tropical Haematology to be established at the Post-Graduate Medical School, Hammersmith, London. A further R 50,000 is being allocated during the next 5 years for the continued support of Dr. Baker's Unit at Vellore, and R 28,000 to organize and maintain a scheme of cooperation, by visits and interchange of research material between research groups and a Royal Army Medical Corps team in Singapore.

During the past 6 months the Wellcome Foundation has distributed an additional R 496,000 for extensive research into the discovery, development and manufacture of drugs and pharmaceutical products.

* * *

SQUIBB MEDICAL FILMS

Squibb Laboratories (Pty.) Ltd. of Isando, Transvaal, announce the addition of the following medical films to their film library:

. . . and the Earth Shall Give Back Life.
Cancer—The Problem of Early Diagnosis.
Congenital Anomalies of the Heart.
Oral Diuretics in Clinical Medicine.
Physiology of the Natural and Synthetic Adrenal Steroids.
The Valiant Heart.
The Problem of Gastro-Intestinal Cancer.

Squibb films are available for private or group showings as a service to the medical profession.

Films may be obtained by getting in touch with the local Squibb representative or by writing direct to the Film Department, Squibb Laboratories (Pty.) Ltd., P.O. Box 48, Isando, Transvaal. (*Telephone*: 975-4614).

* * *

GOLF TOURNAMENT 1961

The Medical Graduates Association annual Golf Tournament took place at Glendower Golf Club on Sunday, 22 October 1961.

The results were as follows:

Winner's Prize: Abbott's Trophy and radio donated by *Abbott Laboratories* won by *Dr. M. Mandelstam.*

Runner-Up: Westdene Trophy donated by *Westdene* and Electric Shaver donated by *Continental Ethicals*, won by *Dr. B. T. Bernstein.*

Best Gross: M. & L. Trophy donated by *M. & L. Laboratories* and prize donated by *Upjohn (Pty.) Ltd.*, won by *Dr. H. Neifeld.*

Best First Nine, Best Second Nine: Ronson Lighters donated by *Bristol Laboratories*, won by *Drs. C. Kisner* and *L. Apter.*

Third Prize: Golf improver donated by *Sterling Drugs*, won by *Dr. V. Gordon.*

2 Club: Golf Balls donated by *Evans Medical*, won by *Drs. M. Mandelstam, B. Bradlow, M. Shapiro.*

Hard Luck: Prize donated by *S.K.F. Laboratories*, won by *Drs. P. Dinner, A. Porter.*

Sweep: Donated by *Johnson and Johnson*, won by *Drs. S. Skapkinker, S. Skudowitz, A. Porter.*

Golf Balls were donated by *Maybaker (S.A.) (Pty.) Ltd.* and *Keatings Pharmaceuticals Ltd.* and used for Consolation Prizes.

Golf tees were given out to each of the players by *Abbott Laboratories; Squibb Laboratories* donated some of their products to each of the players.

Harvey Cohen, *Honorary Secretary.*

* * *

MEDICAL FILMS

Burroughs Wellcome & Co. (South Africa) Ltd. announce that 2 new films have been added to their library:

1. *Fundamental Principles of Immunization.* (16 mm., colour, sound. Running time: 40 minutes).

A presentation of some of the basic principles underlying active and passive immunization of human beings and animals with vaccines and antisera. Methods of producing and testing a wide range of prophylactics are illustrated.

The following main subjects are included. Acquisition of natural and artificial immunity; the phenomenon of primary and secondary stimuli in establishing active immunity; passive immunity; transferred immunity in the new-born child and new-born animals; toxoids and killed bacterial vaccines; living attenuated and killed virus vaccines (1961).

2. *Living with Diabetes.* (16 mm., colour, sound. Running time: 30 minutes).

The film outlines in simple terms the incidence and mechanism of diabetes and describes in some detail how the diabetic can live a normal, active life through diet alone, or through diet and the use of insulin.

The technique of self-injection of insulin is then demonstrated, and is followed by an illustration of the routine urine test. A brief description of the manufacture of insulin is given, and the final sequences provide examples of some causes and symptoms of hypoglycaemia and hyperglycaemia.

The films are available on loan, free of charge, to the medical and allied professions.

Application should be made to Burroughs Wellcome & Co. (S.A.) Ltd., 130 Main Street, Johannesburg. (*Telephone*: 22-7324).

* * *

INTERNATIONAL CONFERENCE ON HEALTH AND HEALTH EDUCATION

PRELIMINARY PROGRAMME

The International Union for Health Education, in collaboration with the World Health Organization, has organized this Conference to be held in Philadelphia, United States of America, 30 June—7 July 1962, on invitation of the American National Council for Health Education of the Public.

The purpose of this Conference is to consider some of the major health problems which confront man in his total environment and to discuss the contribution that health education can make, particularly in enlisting more effectively the participation and support of people in health programmes.

In view of the comprehensive and timely programme that is being planned, it is hoped that the Conference can be well attended by leading health officials and professional workers such as physicians, health education specialists, experts in environmental sanitation, nursing, etc., as well as social scientists, leaders in education, social work and other professions.

Further information about this Conference may be obtained on request from the Secretariat of the Conference at:

1962 International Conference on Health and Health Education,
800 Second Avenue,
New York 17, New York, U.S.A.

PREPARATIONS AND APPLIANCES

ELASE—A NEW HEALING AGENT

Parke, Davis have recently introduced **Elase,** a combination of two proteolytic enzymes to promote the healing of a variety of exudative skin and mucous membrane lesions.

Description: **Elase** combines fibrinolysin (to provide active enzymatic action for fibrin debridement) with desoxyribonuclease (to lyse desoxyribonucleic acid in leucocytes and other nuclear debris).

Ideally, an agent or combination of agents for effective debridement should provide a spectrum of activity sufficiently broad to remove all forms of necrotic tissue; a span of action long enough to eliminate the need for too-frequent dressings; and a sphere of action that confines itself to nonviable material and does not include action on living tissue[1,2]. Although a preparation having all of these characteristics has not yet been developed, considerable interest has been directed recently to the proteolytic enzymes fibrinolysin and desoxyribonuclease derived from bovine sources[1-11] At present the combination of these two enzymes as in **Elase** seems to offer the most promise as an effective debriding agent.

Indications: **Elase** is especially useful for the removal of exudates and necrotic debris issuing from wounds, ulcers or burns, and in the irrigation of abscess cavities, haematomas, sinus tracts and fistulas. It is of similar benefit intravaginally where, among other effects, it promotes rapid removal of necrotic debris associated with vaginitis and cervicitis.

Dosage and Administration: Since the conditions for which **Elase** is helpful vary considerably in severity, dosage must be adjusted to the individual case; however, the following general recommendation can be made:

Topical Uses: Selection of the product form and the duration of treatment must to a great extent be left to the discretion of the physician. It should be clearly understood that after application, the enzymatic activity of **Elase** especially when in solution, becomes rapidly and progressively less and is probably exhausted for all practical purposes at the end of 24 hours.

The dry form and the ointment are stable at room temperature for one year and two years respectively.

Intravaginal Use: Mild to moderate vaginitis and cervicitis—5 ml. of **Elase** Ointment should be deposited by the use of the V-Applicator, deep into the vagina once nightly after retiring, for approximately 5 applications, or until the entire contents of one 30 g. tube

of ointment has been used. Patients should be checked by the physician to determine possible need for further therapy.

Severe Cervicitis and Viginitis: Some physicians prefer initially to instil 10 ml. of the solution intravaginally, waiting one or two minutes for the enzymes to disperse and then inserting a cotton tampon in the vaginal canal. The tampon should be removed the next day, followed by as many courses of **Elase** Ointment as appear necessary. Other physicians have obtained equally good results by using **Elase** Ointment immediately, dispensing with the preliminary use of the solution of **Elase.**

Side Effects: Deleterious side effects have not been a problem at the dose and for the indications recommended. Even at much higher concentrations, side effects have been minimal, consisting entirely of local hyperaemia. The usual precautions against allergic reactions should be observed, particularly in persons highly sensitive to material of bovine origin.

Contra-Indications: **Elase** is not recommended for parenteral use since the bovine fibrinolysin may be antigenic. There are no known contra-indications to topical use as already recommended.

Package Information: **Elase** is supplied in the following forms:

1. A lyophilized powder in sterile vials, each containing 25 units (Loomis) of fibrinolysin and 15,000 units of desoxyribonuclease. The contents of each vial may be reconstituted with 10 ml. of isotonic sodium chloride solution.

2. An ointment in 10 g. tubes containing 10 units of fibrinolysin and 6,666 units of desoxyribonuclease with 0.04 mg. thiomerosal as a preservative in a special petrolatum base. This tube has an elongated nozzle to aid in its application to surface lesions.

3. An ointment in 30 g. tubes, containing 30 units of fibrinolysin and 20,000 units of desoxyribonuclease with 0.12 mg. thiomerosal in a special petrolatum base. This size of tube is particularly suited for the treatment of gynaecological conditions and, if required, separate packages of six disposable 5 ml. vaginal applicators (V-Applicators) are available to facilitate the administration of the proper dose.

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EQUANIL L-A TABLETS

Wyeth Laboratories (Pty) Ltd announce the introduction of **Equanil L-A** Tablets (meprobamate *Prolonged-Release* tablets), an alternative dosage form of familiar **Equanil.**

When the calming, tension-relaxing benefits of tranquillization with **Equanil** must be sustained uninterrupted over a prolonged period of time, this new, long-acting dosage form offers ease and simplicity of administration.

Each continuous-release tablet contains 400 mg. meprobamate made up into specially-coated granules, in a form from which the drug is released over a period of 10 to 12 hours.

Dose: The average adult daily dose is 1 tablet (400 mg.) twice a day, although a dosage range up to 2 tablets twice a day may be required in certain patients. Doses above 2,400 mg. daily are not recommended.

Precaution: Patients taking meprobamate should be warned that their tolerance to alcohol may be lowered, with resultant slowing of reaction time and impairment of judgement and coordination.

Supplied: Bottles of 25.

PRO-ACTIDIL

PROLONGED, SUSTAINED ANTIHISTAMINIC ACTION

Burroughs Wellcome & Co. (South Africa) Ltd. announce the introduction of **Pro-Actidil** and supply the following information:

Pro-Actidil brand Tablets are a new presentation o **Actidil** brand Triprolidine Hydrochloride, the mos potent and safe antihistamine available.

Composition: Each **Pro-Actidil** tablet contains 10 mg. of Triprolidine Hydrochloride divided between 3 layers of a specially devised excipient which provides for a rapid onset of action, followed by a sustained release of the drug to give a therapeutic effect lasting up to 24 hours in most patients.

The outer layer of a **Pro-Actidil** Tablet contains 2.5 mg. Triprolidine Hydrochloride and has a rapid onset of action and duration of effect similar to that of an ordinary **Actidil** Tablet. A good therapeutic level is maintained for 4 to 6 hours.

The intermediate layer contains 5 mg. Triprolidine in a specially-formulated, slowly digestible base. The anti-histamine effect of this layer begins before that of the outer layer has diminished, and lasts for 11 to 12 hours.

The central core, which contains 2.5 mg. Triprolidine, is released towards the end of that time. This last section continues the powerful antihistamine effect for a further 4 to 6 hours.

Indications: **Pro-Actidil** is indicated in all conditions in which a prolonged sustained antihistaminic effect is required, especially in allergic dermatoses, urticaria, seborrhoeic eczema, angioneurotic oedema and pruritus. Other conditions in which **Pro-Actidil** is useful are vasomotor rhinitis, hay fever, particularly nocturnal and early morning attacks, and allergic asthma associated with bronchospasm.

Dosage: For adults, and children over 10 years, one **Pro-Actidil** Tablet should be swallowed *whole* every 24 hours—preferably between 6 and 7 p.m.

Price: Price to public—bottle of 10—R 0.95, i.e. 9½ cents per day.